A BRIEF ORIGINAL CONTRIBUTION

Baldness and Coronary Heart Disease Rates in Men from the Framingham Study

The authors assessed the relation between the extent and progression of baldness and coronary heart disease. Baldness was assessed twice, in 1956 and in 1962, in a cohort of 2,017 men from Framingham, Massachusetts. Extent of baldness was classified in terms of number of bald areas: no areas bald *(n* = 153), one area bald *(n* = 420), two areas bald *(n* = *587*), and all areas bald *(n* = *857*). Men who were assessed both times and who had two or fewer bald areas during the first evaluation were classified into one of three groups: "mild or no progression," "moderate progression," or "rapid progression." The cohort was followed for up to 30 years for new occurrences of coronary heart disease, coronary heart disease death, cardiovascular disease, and death due to any cause. The relations between the extent and progression of baldness and the aforementioned outcomes were assessed using a Cox proportional hazards model, adjusting for age and other known cardiovascular disease risk factors. Extent of baldness was not associated with any of the outcomes. However, the amount of progression of baldness was associated with coronary heart disease occurrence (relative risk (RR) = 2.4, 95% confidence interval (CI) 1.3-4.4), coronary heart disease mortality (RR = 3.8, 95% Cl 1.9-7.7), and all-cause mortality (RR ~_ 2.4, 95% Cl 1.5-3.8). Rapid hair loss may be a marker for coronary heart disease.

alopecia; cardiovascular diseases; coronary disease; men; mortality; risk factors

Epidemiologic studies on the relation between male pattern baldness and coronary heart disease (CHD) risk have produced inconsistent results. Two case-control studies and two cohort studies each of which controlled for CHD risk factors, demonstrated positive associations between baldness and CHD. In a recent case-control study, Lesko et al. found that men with baldness at the crown of the head had the highest risk of CHD. Adjustment for risk factors in their analyses was based on subject self report. Three other case-control studies that did not control for CHD risk factors showed no relation. Overall, these studies suggest that, at most, a small risk of CHD may be associated with baldness. However, only one of the above studies was prospective. None investigated the relation of the progression of baldness to CHD, which was the objective of this report.

MATERIALS AND METHODS

To further evaluate the association between baldness and CHD, we used data from the Framingham Study. Male subjects were biennially followed prospectively for up to 30 years from the time of the initial measurement of extent of baldness, and up to 24 years for progression of baldness, to determine the relation of baldness and its progression to the development of CHD, CHD mortality, CVD mortality, and all-cause mortality.

Since 1948, the Framingham Study has followed 2,336 males and 2,873 females in order to investigate the relations between risk factors and the development of CHD and cardiovascular disease. Risk factors and the development of cardiovascular events were evaluated every 2 years by medical history, medical record review, and physical examination. CHD was defined as angina pectoris, myocardial infarction, coronary insufficiency, or sudden death. Cardiovascular disease included CHD events plus atherosclerosis related disease such as cerebrovascular accidents, transient ischernic attacks, congestive heart failure, and

claudication. All diagnoses were verified without knowledge of risk factors by Framingham examiners who reviewed medical records and death certificates. Approximately 3 percent of the subjects were lost to follow-up for mortality during the first 45 years of the study.

Extent of baldness

Baldness among the Framingham men was evaluated by the examining physicians in 1956 (n = 1,703) and 1962 (n = 1,928). For our analysis, men with cardiovascular disease at the time of the baldness evaluation were excluded. There were 108 and 172 men excluded for this reason in the 1956 and 1962 cohorts, respectively. Baldness was evaluated at least once for 2,017 men. We based our assessment of the extent of baldness or hair loss on the number of bald scalp regions, and we classified the men into four mutually exclusive groups defined as follows: 153 men had no bald areas, 420 had one bald area (front only, sides only, or back only), 587 had two bald areas (front and sides only, front and back only, or sides and back only), and 857 had a degree of baldness in all areas (front, sides, and back) (see figure 1 and table 1). The all-areas-bald category is roughly comparable to the Hamilton baldness scale's Class VIII. Pattern of baldness (e.g., vertex) was not recorded.

The cross-sectional relations between the extent of baldness and CHD risk factors were examined via a general linear model, adjusting for age. The final data set for the mortality outcomes in relation to extent of baldness (after exclusion of men with CHD) consisted of 2,017 men, 1,595 first evaluated in 1956 and an additional 422 first evaluated in 1962. For those examined twice, the baldness evaluation used in this analysis was the first (1956) evaluation. The longitudinal relations between initial extent bf baldness and

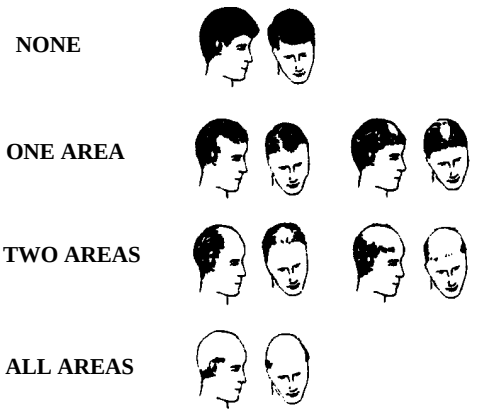

FIGURE 1. Standard classification of baldness used by the authors. (Based on the Hamilton (1) classification.)

TABLE 1. Change in baldness classification* of the 433 Framingham Study cohort members who were examined for baldness in both 1956 and 1962, Framingham, Massachusetts

Baldness classification in 1962	Baldness classification in 1956	
	No areas bald	One area bald
No areas bald	23	37
One area bald	19	47
Two areas bald	44	98
All areas bald	34t	131
Total	**120**	**313**

*** Baldness classification-no areas: no baldness; one area: front only, sides only, or back only; two areas: front and sides, front and back, or sides and back; all areas: front and sides and back.**
t This group of men had rapid progression of baldness.

incidence of subsequent CHD, CHD mortality, cardiovascular mortality, noncardiovascular mortality, and all-cause mortality for up to 30 years of follow-up were investigated using a Cox proportional hazards regression model. In the latter, extent of baldness was entered into the analysis as three dummy variables for the four baldness categories. The no-areas-bald group was used as the reference group. The regression results were adjusted for age and the CHD risk factors. Systolic blood pressure, total serum cholesterol, and mean Metropolitan relative weight were entered as continuous variables, and cigarette smoking, diabetes, and left ventricular hypertrophy were entered as dichotomous variables. These variables have all been defined elsewhere. To test for a trend over the baldness categories, extent of baldness was entered into an age and risk factor-adjusted Cox regression as a four-point variable. The value of the variable represented the number of bald areas.

Agreement of baldness classifications

The reliability of our classification of baldness was assessed by comparing examination disagreement for men examined for baldness in 1956 and 1962 (n = 1,334). Since men may have seasonal hair changes that can account for an apparent increase in hair with time, unexpected changes were defined only as hair gain from two Areas bald to no areas bald, from all areas bald to one area bald, or from all areas bald to no areas bald. The proportion of men with between examination disagreement was 7 percent (29 out of 393) in the two-areas-bald group and 11 percent (56 out of 508) for the all-areas-bald group.

Progression of baldness

The analyses of progression of baldness investigated 433 men who had been examined twice for baldness,

TABLE 2. Baldness classification* at first examination in 1956 or 1962 among men from the Framingham Study cohort, by age, Framingham, Massachusetts

Age group (years)	Baldness classification: No areas bald No.	%	One area bald No.	%	Two areas bald No.	%	All areas bald No.	%	Total No.	%
35-44	85	56	182	43	168	29	159	19	594	29
45-54	45	29	151	36	211	36	284	33	691	34
55-64	20	13	72	17	182	31	315	37	589	29
65-74	3	2	15	4	26	4	99	12	143	7
Total	153	100	420	100	587	100	857	100	2,017	100

Baldness classification-no areas: no baldness; one area: front only, sides only, or back only; two areas: front and sides, front and back, or sides and back; all areas: front and sides and back.

did not have CHD at the time of baldness assessment, and had the potential for hair loss. The specific numbers of men were as follows: 2,297 in the total cohort, 280 excluded for prevalent CHD, 683 excluded because they were only examined once for baldness, and 901 excluded because they had little potential for further hair loss. In this latter group were men who had two or three areas of baldness in 1956. The final cohort of 433 and their progression of baldness is displayed in table 1. Progression was defined as follows. Men who had no hair loss in 1956 and had lost hair in all areas by 1962 were classified as having rapid progression *(n* = 34). Men who had no hair loss in 1956 and had two areas bald by 1962 *(n* = 44) and men who had one area bald in 1956 and had hair loss in all areas by 1962 (n = 131) were classified as having moderate progression (total, *n* = 175). All others were classified as having mild or no progression *(n* = 224). The latter group included men whose extent of baldness did not change, men who had no baldness in 1956 and one area bald in 1962, those who had one area bald in 1956 and progressed to two areas bald, and those who had decreased baldness.

Cox proportional hazards regression was used to evaluate the relation of progression of baldness to incidence of **CHD, CHD mortality, cardiovascular** mortality, noncardiovascular mortality, and all-cause mortality for 24 years of follow-up from 1962 onward. Progression of baldness was entered as two dummy variables, with no progression or mild progression used as the reference group. All regressions were age and CHD risk factor-adjusted.

RESULTS

Baldness was common in men aged 45 years or more (table 2). Of the entire cohort, 857 men (42.5 percent) had all areas bald, 587 (29.1 percent) had two areas bald, 420 (20.8 percent) had one area bald, and 153 (7.6 percent) had no areas bald.

The age-adjusted mean values for extent of baldness were examined in relation to the CHD risk factors. Extent of baldness was significantly related to only one of the CHD risk factors, Metropolitan relative weight (p = 0.028). The Metropolitan relative weights for the men with no areas bald, one area bald, two areas bald, and all areas bald were 120.5, 119.4, 120.4, and 121.9, respectively. There was no consistent pattern in the relation of any of the CHD risk factors to the baldness classifications.

TABLE 3. Age-adjusted rates of cardiovascular events and deaths in a group of Framingham Study men after 30 years of follow-up, by extent of baldness, Framingham, Massachusetts

Outcome	Extent *of* baldness: No areas bald *(n = 153)* No.	Rate*	One area bald *(n = 420)* No.	Rate	Two areas bald *(n = 587)* No.	Rate	Three areas bald *(n = 857)* No.	Rate
All deaths	73	61	219	60	351	60	559	59
CHD T deaths t	33	26	84	23	108	19	183	19
CHD	63	47	149	41	195	35	288	36
CVD T deaths §	39	32	108	31	158	27	274	28
Non-CVD deaths	34	29	ill	29	193	33	285	30

* 30-year rate per 100 patents (age-adjusted).
t CHD, coronary heart disease; CVD, cardiovascular disease.
t Includes myocardial infarclion, angina, and sudden death.
§ Includes coronary heart disease events plus stroke.

TABLE 4. Adjusted* relative risk of a cardiovascular event or death in a group of Framingham Study men after 30 years of follow-up, by extent of baldness, Framingham, Massachusetts

Outcome	Extent of baldness					
	One area bald		Two areas bald		Three areas bald	
	RRt	95% CI T	RR	95% CI	RR	95% CI
All deaths	1.01	0.78-1.32	1.00	0.78-1.30	1.03	0.80-1.32
CHD T deaths t	0.86	0.57-1.29	0.71	0.48-1.06	0.78	0.53-1.14
CHD	0.85	0.63-1.15	0.74	0.55-0.98	0.79	0.60-1.05
CVD T deaths §	0.89	0.61-1.29	0.82	0.58-1.17	0.88	0.63-1.25
Non-CVD deaths	1.14	0.78-1.68	1.21	0.84-1.74	1.18	0.81-1.69

* Adjusted for age and the following risk factors: systolic blood pressure, cholesterol level, weight, smoking, left ventricular hypertrophy, and diabetes status. Men with no areas bald were used as the reference group.
T RR, relative risk; CI, confidence interval; CHD, coronary heart disease; CVD, cardiovascular disease.
t Includes myocardial infarction, angina, and sudden death.
§ Includes coronary heart disease events plus stroke.

Table 3 gives the number of events by extent of baldness. Cumulative 30-year age-adjusted incidence rates for **CHD, CHD** mortality, cardiovascular mortality, noncardiovascular mortality, and all-cause mortality did not show any significant differences in rates across the extent-of-baldness categories. With the no baldness group used as the reference group, Cox regression relative risks for the relations of one, two, and three areas bald to all of the endpoints are given in table 4. Except for CHD morbidity, there was no indication of any statistically significant trends relating risk to extent-of-baldness classification. A trend analysis (see "Materials and Methods") did not confirm a negative relation (p = 0.15) for CHD morbidity. The statistically significant relation of two areas bald with no areas bald (relative risk 0.74, 95 percent confidence interval 0.55-0.98; p 0.04) may be explained as a chance fluctuation.

When age group-specific (35-44, 45-54, 55-64, and 65-74 years) rates of CHD death and incidence were investigated, no statistical difference was found between men who had no areas bald and men who had all areas bald.

The moderate and rapid progression groups showed significantly elevated rates in comparison with the no progression or slight progression group for all out comes except noncardiovascular mortality (table 5). Cox regression analyses were adjusted for age and CHD risk factors. Table 5 shows the number of events and their rates, while table 6 gives the relative risks and 95 percent confidence intervals for the compari sons. For all outcomes, there is a consistent increase in mortality and morbidity when the moderate and rapid progression groups are compared with the no progres sion/mild progression group. These analyses did not include the men who had had two or three areas of baldness in 1956, for they had little opportunity to lose their hair (n = 901). Since we eliminated the men with two areas bald or all areas bald from the analysis, some men who gained hair were not included in the

TABLE 5. Age-adjusted rates of cardiovascular events and deaths in a group of Framingham Study men after 24 years of follow-up, by progression of baldness, Framingham, Massachusetts

Outcome	Progression of baldness					
	Rapid (n = 34) *		Moderate (n = 175)		None or slight (n = 224)	
	No.	Rate T	No.	Rate	No.	Rate
All deaths	22	66	100	54	95	45
CHD t deaths §	11	34	37	20	32	15
CHD	14	47	67	41	60	30
CVD t deaths II	11	34	51	27	41	20
Non-GVD deaths	11	32	49	27	54	26

* n = number of cardiovascular events.
T 24-year rate per 100 patients (age-adjusted).
t CHD, coronary heart disease; CVD, cardiovascular disease.
§ Includes myocardial infarction, angina, and sudden death.
II Includes coronary heart disease event; plus stroke.

TABLE 6. Adjusted* relative risk of a cardiovascular event or death in a group of Framingham Study men after 24 years of follow-up, by progression of baldness, Framingham, Massachusetts

Outcome	Progression of baldness			
	Moderate		Rapid	
	RR T	95% CI T	RR	95% CI
All deaths	1.5	1.1-1.9	2.4	1.5-3.8
CHDt deathst,	1.7	1.0-2.8	3.8	1.9-7.7
CHD	1.8	1.3-2.5	2.4	1.3-4.4
CVDt deaths§	1.8	1.2-2.7	2.9	1.5-5.9
Non-CVD deaths	1.2	0.8-1.8	2.0	1.0-3.8

* Adjusted for age and the following risk factors: systolic blood pressure, cholesterol level, weight, smoking, left ventricular hypertrophy, and diabetes status. Men with slight or no progression of baldness were used as the reference group.
T RR, relative risk; CI, confidence interval; GHD, coronary heart disease; GVD, cardiovascular disease.
t Includes myocardial infarction, angina, and sudden death.
§ Includes coronary heart disease events plus stroke.

referent group shown in table 6. We repeated the analysis with these men included, and the results were similar. Results from the Cox regression models were tested for interaction, such as an interaction between age and progression of baldness. None of these interactions were significant.

DISCUSSION

Our analyses suggest that men who rapidly lose their scalp hair have a greater risk of CHD than men who lose their scalp hair less rapidly. This effect was seen with CHD and cardiovascular outcomes regardless of whether morbidity or mortality was investigated. Our analysis was more thorough than the analyses presented in previous reports, because it used a prospective cohort design, had a 24-year follow-up period, and adjusted for risk factors for cardiovascular disease.

To further test the validity of our conclusions, we investigated other possible explanations for the results. It is unlikely that misclassification of baldness could account for the results seen in this analysis. Since baldness was measured up to 24 years before the CHD event, systematic misclassification bias was unlikely. No information was available on how baldness was classified by the Framingham investigators or on the training of the physician examiners for baldness assessment. Misclassification error was probably nondifferential, and any nondifferential misclassification would bias the results toward a finding of no association. All of our analyses were age-adjusted, so this would tend to have minimized any age bias from the presence of men who had great progression of baldness prior to baseline.

Why did our analysis fail to show a relation between absolute amount of baldness and CHD, while other excellent studies, such as that of Lesko et a1, found such a relation? A closer look at study methods will highlight the reasons. For example, Lesko et al. performed a cross-sectional case-control study, while our study used a prospective cohort. Lesko et al.'s analysis focused on baldness at the time of the CHD event, whereas we examined baldness that was present years before the CHD event. Additionally, case definitions in the two studies were distinct in that our study had a broader case definition than Lesko et al.'s study. For example, our definition of CHD included silent myocardial infarction. The Lesko et al. study investigated separate aspects of the relations between baldness and CHD in comparison with the Framingham analysis.

The literature concerning the biologic processes of baldness is just as varied as the studies of baldness and CHD. Baldness is a prominent characteristic of the aging process in men. We found that 42.5 percent of the men were completely bald, and this agrees with other published results. The development of baldness requires the male sex hormone testosterone. The literature suggests several possible explanations for the links between baldness and CHD; testosterone may be one such link. Smoking's relation to testosterone is one possible explanation for this link. An increase in testosterone levels has been shown to be present in those who smoke. Other studies have found no relation between serum testosterone levels and baldness; thus, they propose that scalp follicles have increased sensitivity to testosterone. Nitric oxide may be another possible link between baldness and CHD. It has been proposed that deficient production of scalp nitric oxide is related to baldness. Moreover, nitric oxide has been associated with control of hypertension, a determinant of CHD (19). There may be a link between genes that control baldness and those that cause atherosclerosis and CHD. Identification of a gene for baldness may help us to identify a gene for atherosclerosis. We were unable to find any publications that could explain why the progression of baldness may be related to CHD. At best, we could speculate that men who rapidly lose their hair are genetically or hormonally different from those who lose their hair more slowly.

We believe that the two strengths of our study, baldness assessment before the CHD events and a 24to 30-year follow-up period, compensate for any misclassification due to the baldness examiners that occurred in 1956 and 1962. If these data are confirmed with results from additional studies, baldness should be considered a marker for CHD, but not its cause. As a marker, progression of baldness may help us to elucidate the etiology of CHD. It may also shed light on why men have a higher rate of coronary disease than premenopausal women. Perhaps a search for the chromosomal location of the baldness gene will also highlight the location of an important atherosclerosis gene. Future research on baldness and CHD should include multiple measures of baldness over time in each man prospectively, and control for associated risk factors for CHD. The above analysis also suggests that the background rate of CHD associated with baldness should be taken into account when evaluating the possible cardiovascular toxicity of hair growth products.